Targeting Medication Nonadherence Using Mobile Phone-Based Tailored Messaging

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ABSTRACT

Purpose: This project sought to design, implement, and assess the effectiveness of tailored messages in changing medication adherence in adults with uncontrolled diabetes using mobile phone delivery.

Scope: Medication nonadherence remains a prevalent public health issue and is especially challenging in patients with diabetes. While multiple approaches have attempted to improve this behavior, results of interventions have been mixed and no single strategy has proven to be universally beneficial. Mobile phone-based methods have become increasingly popular and there is need for deeper individualization of interventions; however, few studies have investigated the delivery of individualized material by mobile devices.

Methods: Messages were guided by items from theory-driven survey instruments. Subjects were recruited from a western Michigan health system and were required to be 21-64 years of age, diagnosed with diabetes, taking at least one antidiabetic medication, and operating a mobile phone. Subjects were randomized to receive one text message per day or standard care only for three months. Survey responses measured changes in health beliefs, adherence was assessed using pharmacy claims, and interviews gathered intervention feedback.

Results: A library of 168 theory-driven and 128 medication-specific messages was created and 48 subjects were randomized. Adherence declined over time in both groups but no significant differences were observed. Unadjusted tests suggested that improvements were made in perceived benefits and competence due to the intervention. The receiving of one message per day was deemed appropriate but respondents indicated that messages tended to still serve as reminders.

Key Words: nonadherence mobile health, diabetes, tailoring

PURPOSE

The rationale behind this body of research is that innovative means of interacting with patients during their treatment are needed, specifically as they relate to their taking of medications for diabetes. Such a need is imperative as historical means to encourage adherence to prescribed therapies have demonstrated limited effect. The application of mobile phone-based communication to the medication taking process is one that is wide-reaching and potentially cost-effective but lacks significant testing and its impact is not fully understood. Moreover, while the individualization of messaging has been applied to medication adherence and other health-related behaviors, few studies have investigated their effect when sent by mobile devices, particularly in patients with diabetes.

Recognizing the need to further test the impact of tailored messages delivered by mobile phone, this study pursued three aims. First, the study sought to demonstrate a means by which condition- and treatment-related tailored messages could be created and formatted for automated delivery by mobile phone. Secondly, the effect of the delivered messages on health beliefs and attitudes, as well as the acceptance of this mode of communication during the treatment process, was pursued. Finally, we sought to examine the impact of tailored text messages on medication adherence in a cohort of adults with uncontrolled diabetes. Collectively, the pursuit of these aims was intended to provide insight on how mobile technology may be applied to the treatment process, the extent to which such communication was accepted, and the impact that tailored material can have on intermediate health outcomes when delivered using wireless technology.

SCOPE

Background

The prevalence of diabetes is a growing public health issue, and rates of disease are expected to continue to climb in the decades ahead. While numerous treatment options exist to treat diabetes, adherence to these medications remains suboptimal in the United States, and such underuse places patients with diabetes at increased risk for poor health outcomes and adds unnecessary costs to the U.S. healthcare system. Multiple interventions have sought to decrease nonadherence in diabetes and other conditions but results have been mixed. The most successful studies have involved the targeting of more than one reason for underuse of medications or have included frequent contact with enrolled subjects. Moreover, the call for improved individualization of approaches has been made in order to more effectively address individual reasons for nonadherence. Resultantly, there is significant need to test low-cost means to individualize interventions, focusing on multiple reasons for nonadherence, and deliver these methods across wide-reaching platforms.

Context

Considered to be communication at its most precise, the tailoring of messages is one means by which an individualized approach can be leveraged to target multiple impacts on a particular behavior. The foundation for tailoring rests in information processing theory where it has been suggested that subjects are more likely to process a message they find more personally relevant. Tailoring has proven effective in multiple behaviors, such as smoking cessation and physical activity, but its application to medication adherence is relatively limited. Fortunately, studies that have applied tailoring techniques to medication use have realized some positive results; however, the vast majority of studies to do so used print or computer-based materials, limiting the ability to easily reach wider audiences in a convenient fashion.

In response to improvements in and the rapid adoption of mobile technologies, interventions have begun leveraging mobile devices in the reaching and motivating of study

subjects to alter particular health-related behaviors. Thus far, studies aiming to improve medication adherence using mobile devices have focused on merely providing reminders to patients to take their medications, limiting their approach to targeting only one reason for nonadherence. A limited number of studies have combined mobile delivery with the tailoring of messages, and those having done so have realized positive effects in multiple instances. However, the use of mobile phone-based tailored messaging has noticeably little experience in encouraging improved medication use in adults with diabetes and deserves further inquiry.

Settings

Subjects for this study were drawn from primary care practices within the Lakeshore Health Network of Muskegon County, Michigan, a wholly owned, physician hospital organization and affiliate of Mercy Health Partners that encompasses over 500 physicians and advance practice providers as well as three hospitals. Muskegon County has a population of nearly 175,000 people and a racial composition similar to that of the entire state of Michigan; however, this region is economically depressed- median household income and the percent living in poverty are worse when compared to the rest of the state. In addition to its economic disadvantage, the Muskegon area has over 16,000 residents diagnosed with diabetes, many of whom have hemoglobin A1c values above 8.5%. Taken together, these suggest that Muskegon was an ideal location to target for behavioral improvement, the insight from which will provide guidance on how mobile interventions may be placed in cohorts of patients with diabetes from disadvantaged regions.

Researchers at the University of Michigan were ideally suited to design and implement this project. The team comprised experts in health behavior and communication, social and administrative pharmacy, clinical pharmacy, and health services research. Perhaps most prominently, resources and expertise were sought through the University of Michigan Center for Health Communication Research, a leader in tailored message design aimed at influencing health-related behaviors.

Participants

In order to be eligible, subjects must have been diagnosed with diabetes, been between 21 and 64 years of age, had a hemoglobin A1c of at least 8.0% (according to their most recent reading), and been taking at least one antidiabetic medication. Additionally, they must have self-reported missing at least one dose in the past 30 days and indicated ownership and operation of a mobile phone. In order to collect medication use information, all subjects must have had continuous enrollment in an insurance plan offered by either Priority Health or Blue Cross Blue Shield of Michigan. Subjects were excluded if they had suffered a heart attack or stroke, been diagnosed with congestive heart failure, or if English was not their primary language.

METHODS

Study Design

This study had two main stages between development and implementation of the intervention. First, all messages for potential use were drafted following an established method developed by experts in tailored message design. Content for the theory-driven messages was drawn from selected survey instruments based on the Health Belief Model and Self-Determination Theory; medication-specific messages were drafted using information from package inserts. Following, initial drafts were reviewed for content and appropriateness by an expert in health behavior and a clinical pharmacist. Two focus groups were also held in the Muskegon area to capture medication-taking and mobile phone use information that may have been specific to the region in order to further alter the study's instruments and messages, if deemed necessary.

Once the message library was finalized, the main pilot study was conducted as a randomized controlled investigation using two arms: an interventional arm that received one tailored text message per day for 90 days and a control arm that received their standard care only. Subjects were randomized once screened and consented using a random number generator. All subjects were compensated with a $50 debit card for their participation at the end of the study; an additional $10 was given to intervention arm subjects who participated in a post-study interview.

Potentially eligible subjects were drawn from the health system's electronic health record system, contacted by mail, and given the option to opt out of being contacted by the study team. Those not opting out were contacted by phone, introduced to the study, and screened for further eligibility, if interest was voiced. Consent to participate was given over the phone and also provided by each subject in writing prior to complete study entry. Subjects were also recruited at an annual diabetes health fair in the Muskegon area during which the study was introduced and interested subjects were screened and consented, if eligible. A subject was considered to be enrolled in the study once the baseline survey instrument was returned. Approval to conduct this investigation was granted by an Institutional Review Board at the University of Michigan and Mercy Health Partners (Muskegon, MI).

Data Sources

Data were collected at multiple points during the study. During the message drafting process, two focus groups were held in the Muskegon area to capture perspectives on medication use and mobile phone operation from adults with diabetes. Questions focused on challenges patients faced during their treatment, ways to improve communication with providers, typical use of mobile phones, and retrieval of health-related information. At baseline, all subjects, regardless of study arm, were given an identical survey. This instrument captured basic demographic information, inquired about general mobile phone operation, and asked subjects to list their current medications, including dose, times per day, and time of day for each dose. The remaining items were adopted from three established, theory-based instruments and focused on patients' health beliefs (instrument developed by Becker and Janz) as well as their self-determination (Treatment Self-Regulation Questionnaire and the Perceived

Competency Scale). Responses to the theory-driven items were scaled (5-point or 7-point Likert) and used to construct tailored, behavioral messages. At study endpoint, subjects were again asked to list their current medications and respond to the same theory-based items; intervention arm subjects were also asked to answer four items based on the Technology Acceptance Model at this time.

To capture medication use information, pharmacy claims data were obtained from two sources. Claims for subjects enrolled in Priority Health were given to the study team directly from the payer; refill information for patients covered by Blue Cross Blue Shield of Michigan was obtained from Lakeshore Health Network. These datasets were combined to calculate overall measures of medication adherence in the two study cohorts for three periods of 90 days each: prior to study entry, active study period, and three month follow-up.

Finally, subjects from the intervention arm were invited to participate in a post-study interview over the phone. Questions focused on the usefulness of the messages they had received, their experience with receiving tailored materials, and future demand or interest in using mobile devices or communication during the treatment process.

Interventions

This study's main focus was on the potential effect of tailored text messages on adherence to diabetes medications. Following randomization, subjects were followed over a period of 90 days, during which time those in the active cohort received one tailored message per day which was automatically delivered to their mobile phone at a pre-specified, fixed time: corresponding to their first dose of the day. The messages focused on two main topics: medication education or health beliefs and motivation. Medication messages focused on either mechanism of action, potential side effects, or demonstrated efficacy and written at the class level for each type of diabetes medication currently approved. Beliefs and motivation messages were constructed using material from established, theory-based items and corresponded to responses given by each subject during in the baseline survey instrument at which time the series of messages to be received was determined by categorizing responses. Regardless of theme, each message also included the subject's name and time of day delivered; other individual attributes occasionally added included the subject's age and mention of a medication they were taking. The result of combining these elements into each message was a deeply tailored message, a level of specificity that the study hoped would be recognized by each subject, thus improving the odds of retention and action as suggested by theory.

A pre-specified rubric dictated the order in which the messages were delivered, rotating between beliefs, motivation, and medication-specific foci. In this manner, subjects were provided encouragement to take their medication as prescribed by either targeting needed areas of improvement such as perceived benefits of treatment, the severity of disease, susceptibility to detrimental health outcomes, internalized motivation, and external forces potentially hindering progress, or by giving additional medication information that may not have been given by a healthcare provider. The messages were structured so that progress could be encouraged based on their initial level for each concept: subjects deemed "low" for a particular item were initially sent messages at that level but were eventually sent a message at

the next higher level in order to make progress more gradual rather than expecting an abrupt shift. It was hypothesized that improvements in at least one health-related belief or attitude would result in enhanced medication adherence.

Measures

To understand the impact of the intervention, two forms of quantitative data were analyzed. Changes in health-related beliefs and attitudes were assessed by ANCOVA using differences between baseline and endpoint responses to the study's survey instrument. Scores related to each construct were summed and an average created to describe subjects' levels, and comparisons were made both within and between cohorts. An overall level of medication adherence was described using the proportion of days covered (PDC) for each of the three study periods. The first fill date for each medication during the 90-day pre-period served as the index date, and for this initial period the number of days between index and the end of the period determined the denominator. For the active study period and the three month follow-up, a 90-day denominator was used. A count of the number of days each medication was on hand determined the numerator (days covered), using the days supply field, and PDC was then calculated as the ratio between total days covered and the days in the period. Both repeated measures ANOVA and ANCOVA analyses were used to compared adherence between groups and assess any changes over time within cohorts. STATA 11.0 (College Station, TX) was used for all analyses.

Limitations

This study was limited in several ways both by the methods used to run the intervention as well as how the outcomes were assessed. First, the sample size was far smaller than had been anticipated and desired, limiting our statistical power to assess main differences in adherence and health beliefs while hindering any ability to conduct sub-group analyses. Secondly, the length of the study may not have been long enough for significant change to have been instilled in the subjects, either in adherence or beliefs. Additionally, the multifaceted nature of medication nonadherence introduces myriad reasons for deviations in prescribed behavior. While well-tested, the theories used to construct each message, and thus influence behavior, may not have targeted the reasons for nonadherence in each individual among this study population, resulting in a smaller effect than would be expected had their main reasons for nonadherence been addressed. Moreover, the study enrolled subjects with either type one or type two diabetes as well as those who had disease for a variable amount of time; therefore, the content of some messages may not have been appropriate for some, limiting the impact of those messages received. Also, while content experts were leveraged, limited input from potential subjects was sought during the message writing process, again limiting the potential applicability of the messages to the population used. Furthermore, the manner of message delivery was such that a message sent could be confirmed but we could not ascertain whether each message was read and understood each time.

The analysis was hindered in two main ways. First, the use of pharmacy claims is an indirect measure of medication use- a prescription filled does not guarantee that medication will be taken. Similarly, the use of the days supply field assumes that the amount supplied corresponded to the actual use; however, some products, such as insulin, may have included instructions for variable use. Secondly, not all subjects had reliable pharmacy claims within their insurance record; therefore, the ability to assess the study's impact on adherence was severely limited. Moreover, many diabetes products are now available through discount generic medication programs, the filling records for which were not available.

RESULTS

Principal Findings

A total of 75 people (out of an initial pool of 400) were consented and randomized into the two study arms; ultimately, 48 participated in the investigation by providing baseline responses to the survey instrument. An equal number of subjects from both genders were involved, the mean age was 47 years (SD: 11.7), most were married, and nearly all participants were either White or African American. Most subjects reported texting 10 times or fewer per day and a majority or enrollees owned smartphones- more regular texting and smartphone ownership was more likely in younger participants. The cohorts were well balanced considering all included characteristics.

The majority of subjects (70%) reported taking one or two medications each day at an average of four doses per day with the number of doses tending to increase with age. Metformin was the most commonly reported medication but insulin (both rapid-acting and long-acting) was also well represented.

Across both groups, mean scores were highest for perceived severity and autonomous regulation, suggesting that subjects were aware of the seriousness of diabetes but also had adopted some internalized, self-motivating behaviors. A negative relationship between the number of medications and perceived barriers ($r = -0.42$, $p=0.004$) was observed and values for external regulation tended to increase with age ($r=0.429$, $p=0.02$).

Following the intervention, interviews were conducted with select members of the intervention arm, the focus of which centered on their impressions of receiving a daily text message, the applicability of the content, and demand for a future texting program, including any suggestions for improving the approach. Twelve subjects were interviewed and their characteristics mirrored those of the general study population. All but one participant enjoyed receiving a daily message, and respondents indicated that each message served as a reminder, provided encouragement, or gave helpful tips. Similarly, nearly all interviewed indicated that the individualization made them more likely to read and thoughtfully consider each message. Those interviewed felt that one message per day was appropriate but many felt that the frequency could match their individual dosing schedules without becoming bothersome. Subjects indicated that a future, similar program could benefit from including two-way communication with providers, the ability to receive feedback based on their current status, and heightened incorporation of material specific to checking sugars as well as diet and

exercise. Both types of messages—motivational and treatment-specific—were well received but most indicated that regardless of content each message still served as a dosing reminder.

Outcomes

Adherence was measured at three time points throughout the study and compared between groups and over time. At baseline, adherence to diabetes medications was relatively high in the active and control arms, 84.4% and 87.1% respectively ($p>0.05$), and most had a baseline PDC of at least 80%. Declines in adherence from baseline were observed in both study groups but no significant differences were determined between the cohorts or across time in either group; however, the decline was less pronounced in the active arm between baseline and endpoint (-5.8% versus -16.4%). ANOVA analysis showed a significant overall time effect ($F(1,18) = 0.03$, $p=0.012$), a non-significant cohort effect, and a non-significant cohort by time effect. The resulting effect size of the intervention was 0.034. It should be noted that these results should be taken with caution as the small sample size of subjects with reliable pharmacy claims ($n=20$) restricted the statistical power of the analysis.

At baseline, no significant differences in any health belief or attitude were determined between cohorts (all $p>0.05$). After adjusting for baseline values, significant differences in all constructs were also lacking at the conclusion of the study. However, unadjusted analyses suggested that significant improvements were realized in intervention arm subjects for perceived benefits and perceived competence (both $p=0.03$). Loss to follow-up was minimal; all but four of the original subjects were included in the final analysis.

Additionally, technology acceptance—as measured in the intervention arm—was relatively high, suggesting that the incorporation of a mobile device to the treatment process was well received and done so with relative ease. Only two subjects indicated some level of disagreement with usefulness items, and only one did so for the items related to ease of use. No significant differences in ease of use or usefulness were found between subjects based on age, gender, number of medications, type of mobile phone, or texting frequency. Correlation analysis indicated that ease of use had a significant, positive relationship with perceived competence ($\rho = 0.6$, $p < 0.01$) and barriers ($\rho = 0.43$, $p = 0.05$).

Discussion

Adherence to medications is a prevalent issue throughout the U.S. healthcare system, and increased attention needs to be paid to this behavior in adults with diabetes. Multiple approaches have been applied to address nonadherence in this condition but results have been varied and no single method has been consistently successful. This study sought to develop a scheme to tailor messages for mobile phone delivery, demonstrate the means to do so, and evaluate the effect of the messages in a cohort of adults whose diabetes was uncontrolled. Further, the investigation aimed to understand the acceptance of such an approach in a population with varied ages, genders, and ethnicities.

The method used to create tailored text messages produced nearly 300 unique messages that focused on either condition- or treatment-related themes or provided medicinal education. With few exceptions (5.6%), messages were conveyed as scheduled using automated delivery, and deviations from the schedule were generally corrected prior to the next scheduled message. In sum, over 2,200 messages were delivered over the course of the study and at minimal cost. Importantly, changes in treatment regimens from baseline were uncommon, suggesting that the three-month study period was mostly suitable for maintaining medication-specific messages without updating to match changes in therapies. As part of the aims of this study, the means to easily tailor and deliver adherence-focused text messages has been sufficiently detailed for future replication. Such an approach will become increasingly applicable and useful as the integration of mobile devices continues to grow. For these purposes, a static message algorithm was applied but future investigations may benefit from varying the manner by which messages are delivered.

Importantly, this study also gathered qualitative information on subjects' perceptions and acceptance of the tailored text messages. By and large, the messages were well received and subjects voiced interest in future participation should a similar program be offered. The challenge remains that even tailored messages still stand to serve as reminders to adhere to therapy rather than achieving their intended purpose: encouraging behavior change by targeting identified barriers or reasons for nonadherence. While reminders may actually serve a purpose to encourage immediate adherence they may not be suitable for instilling long-term behavior change. Moving forward, message development needs to expand its scope beyond what was demonstrated herein, address additional factors, and improve the individualization of messaging.

While this study did not demonstrate a significant effect on medication adherence it did show, although limited, some improvement in particular health-related perceptions. The unadjusted differences in perceived benefits and competence realized by those in the active arm suggests that some messages resonated well with participants, the result of which was, perhaps, a heightened sense of what medications may accomplish throughout the treatment process as well as what one can achieve in terms of self-management. Since the scope of the messages for this study was primarily focused on medication, it would be valuable to assess the extent to which perceived competence could be expanded through the widening of message topics to include those focused on diet, exercise, or blood sugar testing. Future studies should take this into consideration when crafting their message algorithm and intended content. Similarly, the incorporation of messages describing medication mechanism of action and their demonstrated efficacy appears to have had some impact on how patients felt about their medications, and consideration for this should also be made not only by future interventions but among practitioners who have opportunities to provide these details during encounters.

More importantly, larger sample sizes must be recruited so that more reliable and statistically robust data may be obtained and added to the limited set of information that exists on how tailored text messages may impact medication adherence. Presently, the messages used may have had an effect on the study population but were unobserved due to the small sample size or may have been difficult to measure due to the high prevalence of insulin. As the applications of mobile phones increase in the coming decade so too must our means to

appropriately attract subjects willing to provide insight on how best to leverage these devices in the processes of care.

Conclusions

The relaying of tailored materials by mobile phone is a feasible means by which behavioral interventions may be delivered, particularly when addressing the needs of patients with diabetes struggling with remaining adherent to therapy. Considering the dearth of studies combining texting and tailoring as well as the limited significant results from this study, additional and more extensive testing is required to better understand how these techniques can be applied to adults with diabetes. Fortunately, patients appear to be accepting of receiving tailored text messages and see the benefit such communication can have during their treatment. Future studies should expand their tailoring to additional, known reasons for nonadherence and consider the use of active communication and information exchange between patients and providers.

Significance

Relatively few interventions have paired mobile phone delivery with tailored messaging in order to encourage medication adherence, particularly in adults with diabetes. While significant outcomes were limited in this study, the methods used by the intervention may be applied by future studies wishing to tailor text messages with the goal of targeting nonadherence. Furthermore, the library of messages for this study was constructed with the aim of building an ever-increasing repository of messages that may be used throughout the medical community. Results suggest that particular types of messages may be most useful when seeking to interact with patients; future planned testing will confirm these findings. Importantly, this study demonstrated that following theory-driven methods could lead to a successfully implemented intervention when focusing on tailoring to improve medication adherence.

This study also contributes valuable feedback from participants on their experiences with receiving tailored material delivered by mobile phone. Key findings suggest that messaging may be most effective when provided at the outset of treatment or following a significant change in regimen. Also, improved individualization—by increasing the number of factors included in the tailoring—may lead to enhanced services, engagement, and outcomes. Furthermore, adults of all ages with diabetes appear to be accepting of and willing to use their mobile phones during treatment.

Implications

Results from this study suggest that patients seem interested and willing to use mobile devices during their treatment process provided their individual needs are met by these

communication platforms. Healthcare systems and payers should be mindful of what they offer their patients and enrollees when developing and implementing mobile applications and communication channels. These entities should be prepared to offer a wide range of options when attempting to connect with patients and subscribers. At a minimum, secure, two-way communication should be attempted, provided sufficient practitioner support is available. Moreover, developers must have the ability to accommodate individual patient preferences and barriers when constructing systems in order to increase reach and likelihood of participation.

Findings from this study also suggest that, similar to previous investigations, interventions focused on medication adherence need to expand the scope of their attention beyond only a few factors that contribute to underuse. While potentially labor-intensive, researchers must improve the individualization of interventions in order to be truly tailored approaches and to maximize impact. To aid in this, substantial literature exists to guide a variety of condition- and treatment-related foci, and delivery by mobile phones makes for easy and potentially cost-effective communication. With these points in mind it should be feasible to run interventions or provide patient services over a longer period of time in order to match the chronic nature of diabetes and other lifelong conditions.

OUTPUTS

Gatwood J, Balkrishnan R, Erickson SR, An LA, Piette JD, Farris KB. Addressing medication nonadherence by mobile phone: Development and delivery of tailored messages. *Res Soc Admin Pharm* 2014; DOI: 10.1016/j.sapharm.2014.01.00.

Interview response sheet for mobile phone-based intervention